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A PRELIMINARY REPORT ON A METHOD OF INTRACAVITARY INJECTION IN THE TREATMENT OF PULMONARY TUBERCULOSIS

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Introduction

The purpose of this paper is to make known for the first time a new method in the treatment of chronic pulmonary tuberculosis by means of intracavitary injection. To date this treatment in its present form has been developed and used solely by this unit, and it is desirable that others concerned in the institutional treatment of tuberculosis become familiar with its use. With the experience, ideas and co-operation of other units attempting this form of treatment, it is hoped that a better assessment of its value and indications may be made, and that improvements in the technique and underlying principles may be discovered.

As will be seen, in the few cases treated over a relatively short period, some interesting results have been obtained. In spite of all forms of present-day therapy, some patients with chronic tuberculous cavities in the lungs remain infectious and incurable, and are permanently confined to an institution. It is to this class of patient that this form of treatment is applied, after which he shortly becomes non-infectious, and leaves hospital for a more normal and useful life.

Definition

By this method of intracavitary treatment a medium, heated to the liquid state, and containing antibiotic substances in suspension, is injected into a tuberculous cavity wherein it sets, becoming solid, sterilising and obliterating the cavity space and its communicating bronchus.

The History and Evolution of this Form of Treatment

The underlying principles of this method of intracavitary treatment are based on the concepts of Coryllos in his paper in 1936 on "The Mechanics and Biology of Tuberculous Cavities."[1]

The tuberculous cavity, once formed, becomes the site of constant and profuse reproduction of tubercle bacilli. The further behaviour of this cavity, and its effects upon the patient, are thereafter largely determined by the state of the communicating bronchus. This may be: (1) patent, (2) partially stenosed, or (3) completely stenosed and blocked.

(1) *A patent communicating bronchus* allows for ideal aerobic reproductive conditions for tubercle bacilli within the cavity, and for constant assault on remaining healthy lung tissue by bronchial dissemination of these bacilli and their toxic products. Furthermore, it allows for the maintenance of normal

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atmospheric pressure within the cavity, whereas, because of the negative intrapleural and intrathoracic pressure, the environment surrounding the cavity is at less than atmospheric pressure. Thus the cavity tends to remain open or to increase in size.

The thick, inelastic and avascular fibrous-tissue capsule further promotes the patency of the chronic cavity, and, because of the avascularity of this capsule, the enclosed tubercle bacilli are relatively unassailable by present-day antituberculous therapeutic agents.

(Steenken in 1947 assayed the streptomycin content of tuberculous cavities. He found an average content of 7·7 micrograms per c.c. of aspirated material. The range was 1 to 18 micrograms per c.c., but the dose of streptomycin administered was 1·8 to 2 grams daily, and the nature of the cavity investigated, whether acute or chronic, was not specified.[2] A similar assay is about to be undertaken at this institution in conjunction with the present work on intracavitary treatment.)

(2) *A partially stenosed or œdematous communicating bronchus* may give rise to a one-way valve-like action, thus air entering the cavity under pressure cannot escape, and a rapidly enlarging tension cavity is produced.

(3) *A completely stenosed and blocked communicating bronchus* isolates and seals off the chronic cavity, the results of which are:

(*a*) To arrest at once the further bronchogenic spread of tubercle bacilli from the cavity.

(*b*) By absorption of oxygen and increase in the carbon dioxide content of the intracavitary environment, to render such environment inimical to the further reproduction of the strictly aerobic tubercle bacilli.

(*c*) By absorption of air from the cavity, to promote its gradual closure, with inspissation and eventual calcification of its contents.

Thus it is apparent that most favourable results are obtained by complete and permanent occlusion of the communicating bronchus. This may occur during the natural course of the disease, due to cicatrisation and stenosis of the communicating bronchus following on healing of endobronchial disease, or it may occur through kinking of the communicating bronchus as a result of pulmonary distortion, or through pressure from without by enlarged lymphatic glands or encircling fibrosing disease. In this manner the occasional phenomenon of the sudden decrease in size of tuberculous cavities may be explained.

The Principles of the Present Form of Intracavitary Injection

These are threefold, and the first, based on the concepts of Coryllos, is regarded as being the most important.

(1) To obtain the permanent occlusion of the bronchus or bronchi communicating with the cavity.

(2) To sterilise the cavity by eliminating its contained bacilli and other bacteria by the use of present-day antibiotics, together with an anaerobic intracavitary environment; and,

(3) To fill and replace the existing cavity space with a substance that will eventually be absorbed and replaced by fibrous-tissue formation.

In 1938 Hunter and Peill[3] in England published a paper wherein they described a method of intracavitary and intrapulmonary injection of a gelatin

medium containing acriflavine and calcium chloride. They treated 180 cases and claimed considerable success. Three of these cases were fully described and followed up, but two of the three cases when finally reported on had sputum containing tubercle bacilli. Unfortunately these workers did not have the advantages of antibiotic substances used today in the treatment of tuberculosis. The gelatin-acriflavine-calcium chloride medium was injected at a temperature of over 80° Centigrade, which temperature was necessary to maintain the medium in the liquid state. Never more than 16 c.c. were injected at a time, no attempt was made to fill the cavity completely, and consideration was not given or mentioned in the description of the technique, in respect of bringing about occlusion of the communicating bronchus.

In 1939 the method described by Hunter and Peill was attempted at this hospital.[4] The unfortunate results following the inhalation of the scalding-hot medium from the cavity into the bronchial tree led to the abandonment of this form of treatment by this unit until February 1952, when further work was undertaken along these lines following on the finding of a more suitable medium, and a method of introducing it to fill completely a tuberculous lung cavity.

The medium sought was to have a low melting-point, yet to be solid at body temperatures, both in health and in disease. It had to be a vegetable substance, inert, innocuous to and absorbable by body tissues, and was required to allow of suspension in its substance of present-day antibiotics without chemical change or interaction. Such a substance, in the form of hydrogenated (or hardened) ground-nut oil, was found to be a suitable medium fulfilling the above requirements, and it has been used in selected cases up to the present with good results. However, its use and the principles upon which the present form of treatment has developed bear little resemblance to that originally described by Hunter and Peill.

The Application of the Principles of Intracavitary Injection

(1) *The Medium.*—Hydrogenated or hardened ground-nut oil is formed by the catalytic hydrogenation of liquid vegetable ground-nut oil, being the product of the nut *Arachis hypogæa*. The liquid oil is a complex triglyceride with an acid value of 5 and iodine value of 82 to 99, a specific gravity at 15·5° C. of 0·918 to 0·919, and its solidifying point is 0° to 3° C. It contains various proportions of the following fatty acids in a number of molecular orientations,[5,6] viz.:

SATURATED FATTY ACIDS

	%		%
Myristic	·0	Arachidic	2·4
Palmitic	8·3	Behemic	3·1
Stearic	3·1	Lignoceric	1·1

UNSATURATED FATTY ACIDS

	%
Oleic	56·0
Linoleic	26·0

By the process of hydrogenation, using nickel as a catalyst, the unsaturated fatty acids are converted to saturated acids of the same number of carbon atoms in the molecule. The material is hydrogenated to a melting-point of 49° to 50° C., at which point the iodine value is 25 and the oleic acid content is

calculated to be 28 per cent. of all fatty acids present, the remainder being in the form of saturated fatty acids.

The sterilised hardened oil is put up for use in 60-c.c. and 30-c.c. sterile glass containers with rubber stoppers, and in preparation, while the oil is still in the molten state, 4 c.c. and 2 c.c. respectively of lipiodol oil is added and thoroughly shaken up before allowing the medium to set in the containers. This quantity of lipiodol oil has been found to be the minimum required to make possible a radiological study of the subsequent behaviour of the medium in the cavity. Immediately before insertion into the cavity the following quantities of previously mixed sterile preparations of antibiotics are added to the prepared and melted medium:

TABLE No. 1

THE MEDIUM	QUANTITIES
Hardened ground-nut oil (Melted and Sterile)	60 c.c. or 30 c.c.
Lipiodol oil	4 c.c. 2 c.c.
ANTIBIOTICS (*Ready Mixed*)	
Iso-nicotinic acid hydrazide (I.N.H.)	400 mg. 200 mg.
Streptomycin	2 grams 1 gram
Para-amino-salicylic acid (P.A.S.)	2 grams 1 gram
Terramycin, Aureomycin, Chloromycetin } Singly, or together, as indicated by sputum sensitivities, to a total of	1 gram ½ gram

The molten medium with antibiotics in suspension has a setting-point of 104° F. The complete melting-point is 122·3° F., and the incipient fusion-point (that is, when melting just commences) is 111·7° F.

The following is a list of the names of the proprietary preparations used for incorporation in the medium for injection:

(1) Lipiodol oil. 40 per cent. LAFAY.

(2) Para-amino-salicylic acid. PAS-CILAG crystals for injection solutions. 2·4 G. contained in 20-c.c. vial and supplied by Cilag Ltd., Shaffhouse, Switzerland.

(3) Streptomycin. Crystalline dihydrostreptomycin sulphate. 1 G. contained in 10-c.c. vial and supplied by Chas. Pfizer and Co., New York, U.S.A.

(4) Iso-nicotinic acid hydrazide. Crystalline brand of Cotinazin, as supplied by Chas. Pfizer and Co., New York, in 10-c.c. vials containing 100 mg. per vial. or "Rimifon Roche": Supplied by Hoffman le Roche, Basle, Switzerland.

(5) Terramycin. Crystalline terramycin hydrochloride, supplied by Chas. Pfizer and Co., New York, U.S.A. 250 mg. contained in 20-c.c. vials.

(6) Aureomycin. Crystalline surgical aureomycin hydrochloride powder. 5 G. contained in a 50-c.c. vial and supplied by Lederle Laboratories, New York, U.S.A.

(7) Chloromycetin. Chloramphenicol, 250 mg. capsules for oral use, supplied by Parke, Davis and Co., Detroit, U.S.A. (No sterile preparation of chloromycetin was available for use during the period under review, and where possible, an alternative antibiotic was selected from sputum sensitivity tests carried out beforehand.)

With the exception of chloromycetin, all the above are sterile preparations. Penicillin is not incorporated in the medium because of its greater instability at raised temperatures. The required quantities of the antibiotic powders are mixed with the necessary precautions to maintain their sterility, and are stored for future use in the P.A.S. and streptomycin vials in the quantities required for addition to 60 and 30 c.c. respectively of the prepared medium.

(2) *Occlusion of the Communicating Bronchus.*—The medium, with suspended antibiotics, is injected directly through the chest wall into the tuberculous cavity. The cavity is completely filled up to and into the communicating bronchus or bronchi. The cavity space is thus obliterated, the bronchus is occluded, and the cavity is sealed off from the remaining lung tissue. The contained air is displaced through the open bronchus, or, if this is not freely patent on testing, air is aspirated from the cavity as the medium is inserted. Thus anaerobic conditions are established within the cavity, any remaining air is absorbed, and the cavity walls lie in contact with the medium and its contained antibiotics.

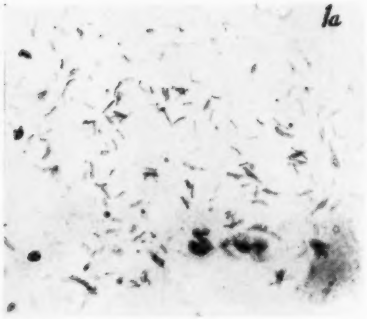
(3) *Sterilisation of the Cavity.*—The anaerobic conditions set up within the cavity are themselves inimical to the growth of tubercle bacilli. The high antibiotic content of the medium is tuberculo- and bacteriostatic and has been found to render the cavity completely sterile. Apart from specific antituberculous drugs incorporated in the medium, oleic acid itself[7] and terramycin[8] are also recognised as being tuberculostatic.

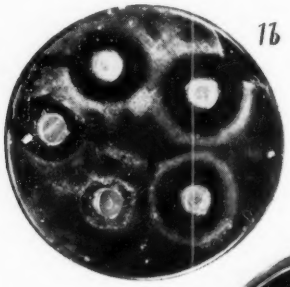
Without exception, in every case in whom intracavitary injection has been successfully carried out, the sputum has become negative for tubercle bacilli both on direct and cultural examination within a period of 4 weeks. This sputum conversion may be accounted for by occlusion of the communicating bronchus alone. However, material subsequently aspirated from the walls of treated cavities has been found to be completely sterile on culture for both tubercle bacilli and secondary organisms (Figs. 1 and 2).

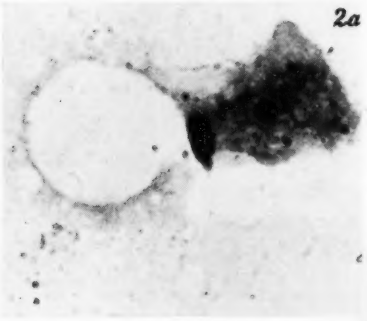
(4) *Obliteration and Closure of the Cavity Space.*—In a suitably selected and correctly treated cavity the medium lies in apposition to the walls of the cavity and acts as a foreign body. This then sets up an acute and chronic inflammatory reaction in the tissues of the surrounding lung and cavity wall. Thus an area of pneumonitis is seen to surround the cavity within a few weeks (see page 17, case 2). Fibroblastic proliferation and ingrowth into the medium with gradual absorption of the latter has led to decrease in cavity size (see cases 1 and 3, pages 18 and 22), and in time ultimate obliteration of the cavity space and its replacement by fibrous tissue is expected.

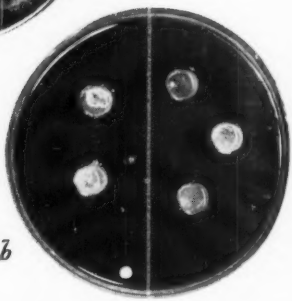
In February 1952 the first patient was treated by intracavitary injection, and as yet in no case has total absorption of the medium with fibrous-tissue replacement occurred. These patients, however, are to date not conscious of or inconvenienced by the presence of the medium in their lungs, and are able to resume normal activities without any discomfort. However, they are advised to avoid the more violent activities such as running or jumping until the greater part of the medium is absorbed.

Cytological examination of material obtained from these patients by bronchial lavage before treatment has invariably demonstrated chronic inflammatory changes, whereas, after treatment, the cytological picture has









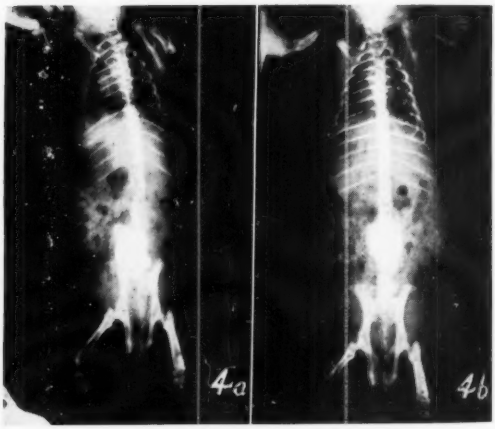


FIG. 1A.—Microphotograph of stained smear of material aspirated from a tuberculous cavity before treatment, showing large numbers of tubercle bacilli.

FIG. 1B.—Photograph of the same material on plate culture, showing growth of secondary organisms and zones of growth inhibition by different antibiotics.[9]

FIG. 2A.—Microphotograph of stained smear of material from the same cavity as in Fig. 1 eight weeks after treatment, showing absence of tubercle bacilli.

FIG. 2B.—Photograph of plate culture of material from the same cavity after treatment, showing absence of growth of secondary organisms.

FIG. 3.—Enlargement of a microphotograph of the cell found on cytological examination of bronchial lavage after intracavitary injection, believed to be a large macrophage containing fat globules. (Magnification ×570.)

FIG. 4A and FIG. 4B.—X-ray of guinea pig immediately after intraperitoneal injection of the medium (4A), and four months later (4B), showing some absorption of the medium and loss of definition of the outline.

become both acute and chronic inflammatory. Furthermore, in every case so examined after treatment a different type of cell has been demonstrated and is believed to be a large macrophage containing fat globules in its cytoplasm (Fig. 3).

Animal Experiments

In preliminary experiments the medium alone, and the medium mixed with antibiotics, were injected intraperitoneally and intrathoracically into guinea pigs and rabbits. These animals suffered no obvious ill effects. Some were killed at various stages and the tissues surrounding the medium examined histologically. These showed adherence of the tissues to the medium with fibroblastic proliferation and infiltration into the medium.

Other animals after injection are being X-rayed at regular intervals. These have shown very gradual decrease in size of the bulk of the medium injected intraperitoneally (Fig. 4), but the rabbit most recently killed and examined showed total absorption of the medium which had been injected intrathoracically, only a fibrous-tissue scar remaining and causing adherence of the pericardium to the diaphragm.

The Procedure and Technique for Intracavitary Injection

(1) *Preliminary Sensitivity Tests.*—Each patient selected for intracavitary treatment is tested routinely for sensitivity to cocaine, decicain and iodine (potassium iodide). In the event of sensitivity to cocaine, sensitivity tests for alternate drugs such as "Xylocaine" or "Nupercaine" are carried out.

(2) *Pleural Symphysis* (or Pleurodesis).—Breakfast is withheld and the patient given Nembutal gr. 3 half an hour beforehand. In the same manner as for inducing artificial pneumothorax, a free pleural space is sought anteriorly, laterally and posteriorly over that part of the lung in which the cavity is situated. Care is taken during this procedure to avoid penetration of the visceral pleura. In this connection, in local infiltration and introduction of the Kuss induction needle used, the sharp needle and stilette respectively are permitted to advance no further than the level of the upper border of the rib. Thereafter the blunt stilette of the induction needle is used to penetrate deeper and through the parietal pleura. In this manner a possible tuberculous empyema, caused by penetration into an active subpleural tuberculous focus, is prevented as far as possible.

Where a free pleural space is located (as is generally the case), 10 c.c. of a ready-mixed solution consisting of 1 per cent. iodine in 50 per cent. sterile glucose is run into the pleural space. This solution is made up as follows:

Glucose 50 per cent. sterile soln.	9 c.c.
Iodine solution	1 c.c.
Iodine	10 grams
Potassium iodide	10 grams
Aq. dest.	100 c.c.

The patient's reaction to this intrapleural instillation is unpredictable. Owing to variations in the pain threshold and pleural sensitivity in different patients, varying degrees of pain and reaction are obtained. Some do not complain of any discomfort, whereas others experience the most severe pain accompanied by evidence of extreme shock. The period of severe reaction,

when it does occur, seldom lasts more than three-quarters of an hour and, depending upon the severity of the pain, so pethedine, morphine, or if necessary light general anæsthesia may be administered. In some cases 2 c.c. of decicain were instilled into the pleural space to attempt alleviation of the severe pain, but this is now avoided as the iodine is precipitated out of solution by the hydrochloride of the decicain hydrochloride solution.

Immediately after running in the glucose-iodine solution the patient is postured in such a manner as to cause pooling of the intrapleural solution over the site of that part of the lung containing the cavity to be injected, both anteriorly and posteriorly, for twenty-four hours, in order to obtain maximum chemical pleuritis and symphysis over that site for later safe needling of the lung.

After two weeks the patient is retested for free pleuræ. If no space is found, and pleural symphysis is assured anteriorly, laterally and posteriorly, intracavitary injection may then be performed. If on retesting a free pleural space is found still to exist (not infrequently the case), depending on the nature of the reaction to the first instillation, a $1\frac{1}{2}$ or 2 per cent. solution of iodine in 50 per cent glucose may be instilled. If the initial reaction was very severe, or if the patient is sensitive to iodine, then 20 c.c. or more of the patient's own fresh blood is transfused from the arm into the pleural space. A solution of glucose, as near saturated as to be able to be sterilised without caramelisation, may also be tried.

Pleural symphysis has been obtained in one case of previous contralateral thoracoplasty, and in another of contralateral upper and middle lobectomy. In such cases acute pleuritis is to be avoided owing to possible reflex bronchospasm, pulmonary œdema and ensuing acute respiratory insufficiency, and intrapleural instillation of the patient's own fresh blood is found to be the most suitable agent. This causes the least pleural reaction, and symphysis may be obtained after one or two attempts.

On one occasion only, pleural symphysis was attempted by the use of sterile talc powder in suspension in a 50 per cent. glucose solution. Fortunately this patient was a strong, well-built male with small bilateral apical cavities and minimal disease elsewhere in the lungs. Symphysis was assured, but the grossly severe reaction lasting one week, with bilateral reflex bronchospasm, pulmonary œdema, shock and respiratory distress would have been, in a less healthy patient with more extensive disease, undoubtedly fatal. This method has, therefore, not been repeated and is not recommended.

Brock,[10] in discussing the treatment of spontaneous pneumothorax, mentions various substances, including glucose and blood, used for inducing a chemical pleuritis and subsequent pleural symphysis. It is his opinion that, in spite of the severe reaction which can be controlled and alleviated, in the long run silver nitrate is the agent of choice and gives the most satisfactory results. However, in the present work the use of silver nitrate solution or other agents causing a very severe reaction has been avoided for several reasons. Many cases selected for treatment have extensive bilateral disease and cavitation, and their general condition is very poor. The severe reaction to silver nitrate would be most detrimental in these cases. Also, the sclerosing action of this substance on the visceral pleura overlying subpleural active tuberculous foci is regarded as

dangerous, owing to the risk of causing a tuberculous empyema. Furthermore, the large number of patients in whom intracavitary treatment is an indicated procedure requires the induction of pleural symphysis on a large scale. As many as seventeen patients have received intrapleural instillation in the same ward on the same day. Simultaneous severe reactions in these patients would place this treatment in disrepute, and, whereas it is now demanded, whether suitable or not, it would shortly be refused.

Considerable difficulty and delay have been experienced in obtaining pleural symphysis before intracavitary injection may be attempted. In some cases it is achieved after the first instillation, in others two or three instillations are required. However, with patience and by varying the quantities, strength and type of agent used, successful results are usually obtained. Further aspects on the subject of pleural symphysis will be mentioned under the later heading on general discussion.

(3) *Preliminary Investigations.*—The size, shape and situation of the cavity are ascertained as exactly as possible by radiography, including tomography. Bronchography is of value in this respect, and if necessary intracavitary injection of lipiodol oil will demonstrate exactly the limits of the cavity and the nature of the communicating bronchus. The mean diameter of the cavity is ascertained by measurement of P.A. and lateral tomograms and the approximate capacity of the cavity calculated mathematically.

The average twenty-four hour sputum output is measured, and sputum is sent for culture for secondary organisms and their sensitivity to various antibiotics. The antibiotic of choice is included in the medium for injection.

Red, white and differential blood counts are done and the hæmoglobin content and prothrombin index estimated.

As soon as possible before intracavitary injection is undertaken a complete clinical examination is carried out, with special reference to the respiratory system. This routine is of value in assessing the nature of any ensuing complication.

(4) *Premedication.*—Breakfast is withheld. During the procedure the patient's full co-operation is required, therefore only light premedication is given. Immediately before being sent to the theatre, the patient is given 2 drachms of linctus heroin and, depending on his response to the drug, $1\frac{1}{2}$ to 3 grains of nembutal.

(5) *The Procedure.*—The patient is first screened in the upright position, and using a skin pencil with a metal pointer attached (pen nib), the selected sites of approach to the cavity are marked anteriorly and posteriorly. These points are then joined by lines drawn across the shoulder and around the chest to act as direction guides in location of the cavity.

After screening, a slow and thorough throat spray and bronchial inhalation is administered using cocaine hydrochloride 5 per cent. or decicain hydrochloride 2 per cent. solutions. This is most important to assist in obtaining suppression of coughing and bronchial irritability, and as a preparation for emergency bronchoscopy if such should become necessary.

Depending on the situation of the cavity to be injected, the patient is placed upon the table to sit or lie in such a position that the cavity is in the lowest position in relation to the rest of the lung with the site of the communicating bronchus uppermost in relation to its point of entry to the cavity.

The skin over the site selected for needling is cleaned with ether and the skin and deeper tissues infiltrated with procaine hydrochloride 2 per cent. or other local anæsthetic.

A thin-gauge 4-inch steel needle attached to an all-glass 10-c.c. Yale B.D. Lock syringe containing 3 c.c. sterile saline solution is used for exploring the chest and locating the cavity. All air is expelled from the syringe and the needle advanced one-eighth of an inch at a time in the direction of the cavity as indicated by the skin markings made on screening. After each advance of the needle the plunger of the syringe is withdrawn. If a blood vessel is pierced blood enters the syringe, whereupon the needle must be withdrawn and reinserted from another direction. Air bubbles entering the syringe against resistance indicate a loose connection, or the needle to be in alveolar lung tissue. Free entry of air into the syringe indicates the point of the needle to be in the cavity, or in a large bronchus, or in a pleural space. In order to obtain the maximum sensitivity of touch gloves are not worn. Immediately prior to the point of the needle entering an air-containing space a sense of resistance to the advance of the needle is felt to give way suddenly as the cavity or bronchus is entered.

At this point the syringe is detached and 2 c.c. of 2 per cent. decicain solution with $\frac{1}{2}$ c.c. methylene blue is injected. If the needle is in a bronchus the patient will cough at once. The shadows of the needle cast on to the patient's chest by two lights in different positions are marked with a skin pencil by an assistant, and after noting the exact depth and direction of the exploring needle, it is then withdrawn. The patient is now postured in the opposite position with the cavity-communicating bronchus downmost, and he is instructed to cough gently. If the communicating bronchus is widely patent he will at once cough up all or most of the dark-blue-stained decicain and further desensitise his bronchi. If the communicating bronchus is blocked or partly occluded, no sputum or only slightly stained sputum will be coughed up.

The patient is now postured in his original position exactly as before. A small skin incision is made over the point of entry of the exploring needle, and a specially adapted Geerling two-way A.P. induction needle with one limb connected to a manometer is driven into the chest. The exact direction is indicated by lining up the shadows of the needle with the most recently drawn skin markings, and penetration, as indicated by exploratory needling, is made to the same depth to enter the cavity. The stilette is withdrawn, the needle quickly closed and the manometer oscillations observed. Predominantly negative oscillations indicate the needle to be in a free pleural space or in a "closed" cavity under reduced pressure. In the latter case careful admission of a few c.c. of air through the needle will impart a positive element to the manometer swing, whereas if in a pleural space the admission of a small quantity of air will not materially alter the character of the swing, when the needle must be withdrawn and the procedure discontinued pending reassessment.

When the above precautions have been taken to ensure that the needle is neither in a blood vessel, in a free pleural space, nor in a large bronchus, the main limb of the needle is opened and air allowed to enter or leave the cavity to equalise the intracavitary pressure with that of the outside environment. The main limb of the needle is again closed and the manometer observed. In

the case of a thin-walled cavity with a widely patent bronchus the manometer swing will be small, usually plus 3—minus 3 to plus 4—minus 4. If the cavity be thick-walled the swing will be smaller. This, in conjunction with the free expectoration of the previously instilled methylene blue, confirms the wide patency of the bronchus. A cavity with a blocked or partly stenosed bronchus will give an increased manometer swing with the emphasis on the negative element. If air is aspirated from such a cavity by means of a syringe attached to the main limb of the needle, and until the manometer reads in the region of minus 12, in the case of a narrowed bronchus the negative element will tend to become reduced, whereas in the case of a completely occluded bronchus it will be maintained. Confirmatory evidence of such conditions in the bronchus are provided by the expectoration previously of slightly stained or unstained sputum after methylene blue injection.

It is important to have knowledge of the above factors before beginning injection into the cavity. In the case of an " open " cavity air is displaced via the open bronchus as the medium is injected, whereas in dealing with a " closed " or " partially closed " cavity, the displaced air must be aspirated from the uppermost point of the cavity. If this is not done the cavity will be ruptured, or the forced passage of air through the stenosed bronchus will result in coughing, which at this stage is most undesirable. In the case of " closed " cavities, as the medium is inserted air may be aspirated via the same needle, provided that the needle point can be positioned at the uppermost part of the cavity in close proximity to the bronchus. If such a position cannot be ensured, then a second wide-bore needle must be inserted into the cavity at its uppermost point, by means of which air may be displaced until the cavity is completely filled with the medium.

After the state of the communicating bronchus has been ascertained, the depth of the cavity is explored by inserting the needle as far as possible into the cavity without interference with the free flow of air in or out of the needle. Any pus or caseous material aspirated during this procedure is retained for laboratory investigations. The point of the needle is then positioned as required in the cavity and set by means of the sliding stop on the needle shaft. The cavity is now ready for injection with the medium.

In a suitable receptacle, previously warmed, the ready-mixed antibiotics are stirred into suspension into the cooled but still molten medium. The whole quantity is then drawn up into a heated 50-c.c. Yale B.D. Lock all-glass syringe fitted with an adaptor to a "Record" type nozzle. The mixed medium is allowed to cool further in the syringe until its temperature and consistency will allow for the very slow injection of the total quantity into the cavity, wherein it must set almost immediately on entering. Very often the molten medium, on contact with the colder metal of the needle, sets in and blocks the bore of the needle immediately injection commences. This is easily rectified by removing the syringe and clearing the needle-bore by inserting the stilette. It is advisable to inject the first few c.c. of the medium at a more rapid rate in order to increase the temperature of the needle quickly without setting of the medium in the needle-bore. The correct time to begin injection can only be judged after practice. In this respect, injection of the medium into the warmed rubber bulb of an enema syringe has been found helpful, the bulb representing the

cavity, and the rubber outlet tube the communicating bronchus. Too early injection results in most of the medium remaining fluid in the cavity over a considerable period. During this time, if the patient should cough or to the slightest extent raise his intrathoracic pressure, the molten medium may be forcefully expelled into the bronchial tree, where it sets with ensuing generalised bronchial obstruction. This results in further uncontrollable coughing and expulsion of more medium into the bronchial tree, thus establishing a vicious circle over which one has no control. On the other hand, commencing injection too late results in setting of the medium in the syringe. Once this occurs it must be discarded. The medium cannot be reheated to the molten state, as the temperature required for this purpose will destroy the antibiotic properties of and cause chemical changes in the suspended antibiotics. The medium in the molten state with suspended mixed antibiotics is yellow in colour. Should a brownish colour appear the indication is that the antibiotics in the molten medium have been subjected to too high a temperature and the mixed medium must be discarded.

It is possible to draw into the syringe and inject smaller quantities of the mixed medium at a time. This method is suitable when the point of the needle can be assured to be at the uppermost point of the cavity. However, if this is not possible this practice will result in the medium in the cavity setting hard about the point of the needle. When this occurs further injection is prevented, and the needle must be withdrawn and reinserted into the cavity above the level of the set medium, a procedure which is usually more difficult. Once the level of the medium in the cavity rises above the point of the needle, injection is continued more slowly to assure adequate setting of the medium, yet retaining sufficient viscosity to allow for complete filling of the cavity.

Very slow injection of the medium is continued until air can no longer be aspirated from the cavity from a point in close proximity to the communicating bronchus. Injection is now discontinued and time is allowed to ensure that the medium in the cavity sets and becomes solid throughout. During this period every method of persuasion is used to prevent the patient from coughing or raising his intrathoracic pressure in any way whatsoever. When sufficient time has passed and the medium in the cavity judged to be set solid (again a matter of practice), the needle nearest the opening to the communicating bronchus is cleared with the stilette, and a further slow injection is undertaken until the patient indicates any sensation or tickling in the throat or bronchus. Such indication must be made by movement of the head or hand, and indicates that the medium has filled the communicating bronchus and overflowed into the main bronchus. Further injection is at once discontinued and the patient encouraged to breathe quietly through the mouth, and if possible not to cough for several minutes or longer to ensure hardening of the medium. This procedure has been found to be quite satisfactory provided the previous bronchial cocaine inhalation has been sufficiently thorough. After sufficient time has elapsed the patient is now told to cough once or twice, which results in the expectoration of the small quantity of hardened blue-stained medium that has overflowed from the communicating bronchus. If the overflow has been too great, which should not be allowed to happen, a large piece of set medium may be unable to pass the vocal cords, whereupon it must be removed by bronchoscopy.

if coughing cannot be prevented during the final injection, further injection is now usually out of the question, and the needle should be withdrawn from the chest. The small quantity of medium from the final injection is expelled by coughing, but the main body of the medium in the cavity, and for a short distance in the communicating bronchus, is safely set and hardening.

As the injection needle is withdrawn a small quantity of medium is injected along the needle track. This serves to prevent egress of infected material from the cavity into surrounding lung tissues, or the forced passage of any remaining air from the cavity causing surgical emphysema of the surrounding tissues. The chest is now carefully auscultated, and any rhonchi or other adventitious findings not present on auscultation immediately before injection was commenced, or any suggestion of the presence of bronchial obstruction or foreign body, are indications for immediate and urgent bronchoscopy.

On completion of intracavitary injection the patient is X-rayed for examination of the treated cavity. In this respect penetrated P.A. and lateral views taken with a Lysolin grid have proved most helpful towards demonstrating the finer details of the cavity and the contained opaque medium.

(6) *Post-operative Routine.*—On return to the ward the patient is suitably postured to place the treated cavity in a dependent position in relation to the rest of the lung. This posture is maintained for as long as possible. For example, for a right upper lobe cavity the patient is encouraged to lie on his right side and the foot of his bed is raised 18 inches on blocks. For the first month they are allowed " bathroom privileges " only. Thereafter they are allowed up but are encouraged to remain on posture for as long as possible apart from ordinary " rest hours."

For the first week after treatment coughing is discouraged and if necessary suppressed with linctus heroin or syrup codeine phosphate, and the average twenty-four-hour sputum output is measured during the second week.

Monthly X-ray, penetrated X-ray of the chest and tomography of the treated lobe are carried out to record and study the behaviour of the medium and the response of the cavity and remaining lung fields. Bronchoscopy is performed at three-monthly intervals.

The Intracavitary Injection Needle

The needle used for intracavitary injection is an adaptation of the Geerling two-way A.P. induction needle (Gurr, Johannesburg) with detachable screw-on needle and needle hub, whereby the instrument is converted into a trochar and cannula with a side arm and taps as illustrated in Figs. 5, 6 and 7).

The original needle is removed from the screw-on needle hub, the bore of which is enlarged and fitted with 4-inch 13-gauge exploring-type needle (Gurr, Ref. No. 340) the cutting point of which is squared off and sharpened to a gradual and fine taper with the stilette. A second needle hub is similarly adapted for the same instrument, but the length of the needle fitted is cut down to $2\frac{1}{2}$ inches for use in cavities situated close to the chest wall. Two stainless-steel stilettes are made to fit exactly the bore of the needle shaft, and of different lengths to fit the assembled instrument with 4-inch and $2\frac{1}{2}$-inch needles respectively. The needle is completed by fitting to the needle shaft an adjustable stop with fixing-screw. By means of the latter, when the needle point is in the

cavity and the stop adjusted against the chest wall, the needle cannot be driven further into the chest than is intended during injection of the medium.

A 14-inch length of translucent rubber is fitted with the necessary adapters to connect the side limb of the needle with the tubing leading to the manometer. This tube is sterilised with the instruments used and enables the operator to avoid handling unsterile tubing connected with the manometer.

It is occasionally necessary to insert a second needle into the cavity for aspiration of displaced air and final injection of the medium. For this purpose a similar needle to the above may be used, but in this case the side limb and taps are redundant and also often in the way of the operator. Therefore a second 13-gauge needle is constructed of exactly the same dimensions as those described above, but having a stilette and no other encumbrances.

Facilities required for Intracavitary Injection

In this hospital the operation is performed in a subsidiary X-ray and screening room adjoining the main operating theatres, where facilities and instruments for bronchoscopy and bronchial foreign-body removal are immediately available. Oxygen and equipment for its administration are maintained ready for use if necessary throughout the operation.

The table used is a combined screening and X-ray table which can be tilted to the vertical or horizontal positions, and is fitted with a Potter-Bucky diaphragm. By means of this table the patient may be suitably postured, and if at any time during the operation doubt exists regarding the position of the needle or other conditions within the chest, immediate screening or lateral or P.A. X-ray may be undertaken without removing the needle or altering the position of the patient.

A hand basin and steam steriliser are fitted, from which a convenient supply of hot and cold water is available for melting and adjusting the temperature of the medium.

Case Reports

Three cases treated by intracavitary injection are reported, Case 1 being the first to receive treatment by this method.

CASE 1. An African male, aged 27 years.

May 1948. Admitted to hospital with bilateral upper lobe cavitation and generalised miliary spread throughout both lungs. Sputum positive for tubercle bacilli, E.S.R. 22 m.m./hour, general condition fair, weight 121 lb. Treated by diet and postural bed-rest. Pneumoperitoneum was induced in January 1949. In September of that year the patient absconded from hospital.

January 1950. Readmitted to hospital. X-ray showed considerable increase in size of both upper lobe cavities. The original miliary spread was no longer obvious, but there was now bronchogenic spread of the disease into the right lung. His sputum was heavily positive, and he was again treated by diet and postural bed-rest, to which para-amino-salicylic acid and Conteben was added in November 1950, the latter being discontinued in June 1951.

April 1951. There was deterioration in the patient's condition. Both upper lobe cavities had increased in size with increase in the bronchogenic spread on the right. The sputum remained heavily infected with tubercle bacilli which were sensitive to streptomycin, and a severe tuberculous laryngitis had

FIG. 5.—The intracavitary injection needle, assembled with long needle and stilette, with shorter needle and stilette above. One-third size.

FIG. 6.—A, Exploring needle and syringe. B, Intracavitary injection needle with 50-c.c. syringe and manometer tubing attached. (Approximately two-ninths actual size.)

FIG. 7.—Exploded view of the intracavitary injection needle as in Fig. 6. (Two-thirds actual size.) A, main and side limbs with taps; B, stilette; C, screw-on needle; D, adjustable stop with fixing-screw.

FIG. 8.—The instrument trolley and manometer as set for intracavitary injection.

developed. Streptomycin was added to his treatment, at first 1 gram every day for fourteen days, thereafter 1 gram every third day. The X-ray of his chest at this stage is illustrated in Fig. 10.

January 1952. His general condition had now considerably improved. He was afebrile, weight 121 lb., E.S.R. 24 mm./hour and his sputum was still positive. The tuberculous laryngitis had completely resolved, leaving gross residual erosion of the epiglottis and vocal cords. On postural bed-rest with streptomycin and P.A.S. the bronchogenic spread of the disease in the right lung was clearing and both upper lobe cavities had decreased in size (Fig. 11). He had been a restless and unsatisfactory patient throughout, and it was feared

FIG. 9.—Lateral X-ray taken during the operation, showing the needle *in situ* with the medium below.

that he would, in all probability, abscond from hospital a second time. He was considered unsuitable for any other form of treatment, and it was therefore decided to attempt intracavitary injection of the upper lobe cavities.

February 29, 1952. The right upper lobe cavity was treated by injection and was successfully filled in one operation.

March 8, 1952. The left upper lobe cavity was injected, but premature and uncontrollable coughing resulted in temporary abandonment of the procedure with incomplete filling of the cavity.

March 15, 1952. A second injection into the left upper lobe cavity was successful and complete filling was achieved (Figs. 12 and 13).

There was slight blood-staining of the sputum for two days after the first injection into the left cavity, otherwise there was no reaction or complication.

After completion of treatment a few small bronchial casts were expectorated, consisting of the solid medium. Treatment on streptomycin, P.A.S. and postural bed-rest was continued.

April 30, 1952. Sputum examination for tubercle bacilli was negative both direct and on culture. The average twenty-four-hour sputum output had decreased from $5\frac{1}{2}$ oz. to $1\frac{1}{2}$ oz. after treatment.

August 1952. There was marked improvement in the general condition of the patient. He now weighed 128 lb., and his E.S.R. was 18 mm./hour. The sputum, bronchial lavage and gastric lavage remained negative on direct and cultural examination for tubercle bacilli, and the X-ray showed decrease in both cavities with diminution of the bulk of the medium and improvement in the remaining lung fields.

December 1952. Improvement maintained. Weight now 132 lb., E.S.R. 12 mm./hour. The patient has been attending full-time occupational therapy and rehabilitation for the last two months pending his discharge from hospital. He has a persistent harsh dry cough for which no cause can be found other than the residual scarring of the vocal cords and epiglottis from the old laryngitis.

All examinations remain negative for tubercle bacilli, and the lung cavities show decrease in size by half on the right and by two-thirds on the left (Figs. 14 and 15).

In order to ensure follow-up examinations on this patient, he is to be given employment in light work on the African staff of this hospital.

CASE 2. A European female, aged 21 years, unmarried.

December 1951. Admitted to this hospital with pulmonary tuberculosis affecting both lungs, and cavitation known to have been present in the left upper lobe since March 1950, since which time sputum examinations in another hospital were persistently positive. On admission she was febrile (102·6° F.), in poor general condition, weighing 116 lb., and her E.S.R. was 22 mm./hour.

Treatment was commenced with postural bed-rest, P.A.S. 12 grams daily and streptomycin 1 gram daily for sixty days, thereafter 1 gram every third day.

On the third day after commencement of treatment her temperature subsided to normal.

March 1952. There was only slight improvement in the general condition, her weight was 117 lb., E.S.R. was 16 mm./hour and her sputum remained positive. Radiologically there was some improvement evident in the lungs, but the cavity in the left upper lobe showed no change (Fig. 16). Surgical resection of the cavitated lobe was impracticable, due to active disease elsewhere, and in view of her poor general condition and slow response to treatment she was recommended for intracavitary injection.

April 1, 1952. The left upper lobe cavity was treated by injection and completely filled in one operation (Fig. 17). The patient was very co-operative and during the final stage of the injection indicated the overflow of medium into her main bronchus. Coughing was prevented and time allowed for the medium to set, whereupon she was able to expel the small quantity of hardened overflow medium from the bronchus. No bronchoscopy was required.

April 3, 1952. The patient complained of a dull aching pain over the whole of the left chest. She was pyrexial (up to 104° F.), and on examination dullness and diminished breath sounds were present anteriorly and posteriorly over the left chest. There was a polymorphonuclear leucocytosis of 20,000 and examination of the sputum demonstrated large numbers of non-hæmolytic streptococci

FIG. 10.—*April* 1951.

FIG. 11.—*January* 1952.

Case 1: X-ray photographs showing extent of clearing of bronchogenic disease on the right with some closure of the large upper lobe cavities after ten months on treatment with streptomycin, P.A.S., and postural bed-rest.

FIG. 12.—*March* 1952.

FIG. 13.—*March* 1952.

Case 1: Ordinary P.A. immediately after completion of intracavitary treatment (*1c*), showing loss of definition of medium in the right cavity and surrounding area of pneumonitis. Fig. 13 shows tomography of the upper lobes at 7 and 9 cm. depth.

FIG. 14.—*December* 1952.

FIG. 15.—*December* 1952.

Case 1: X-ray and tomography showing closure of cavities, absorption of medium and clearing of the lung fields.

sensitive to streptomycin, chloromycetin and penicillin. The condition was thought to be due to secondary infection following needling of the lung, and streptomycin administration was increased to 1 gram daily and augmented by chloromycetin and penicillin.

April 18, 1952. The pain had subsided, but herpes febrilis was present, due to persisting pyrexia, and she was losing weight and her general condition deteriorating. Examination of the sputum was now for the first time negative for tubercle bacilli on direct and cultural examination. Nevertheless, treatment was commenced with 400 mg. daily of iso-nicotinic acid hydrazide.

X-ray of the chest at this time revealed a homogeneous shadow obscuring the whole of the left base (Fig. 18). Exploratory needling in the region of the left base revealed the presence of a hæmothorax, and 1 pint of blood was aspirated. During the following two days there was a sharp fall in the temperature and thereafter a gradual return to normal.

May 29, 1952. The general condition of the patient had much improved, although she had lost 11 lb. in weight due to the febrile episode. Her temperature had now been normal for the last three weeks. Her sputum had considerably decreased in quantity and remained negative for tubercle bacilli. General treatment was continuing on postural bed-rest, streptomycin 1 gram every third day and I.N.H. 400 mg. daily.

X-ray showed clearing of the shadow over the left base and loss of definition of the edge of the medium in the cavity. Immediately surrounding the cavity a hazy area of pneumonitis was evident (Fig. 19).

October, 1952. Condition very much improved. Her weight before treatment had been regained, her E.S.R. was 12 mm./hour and her sputum, bronchial and gastric lavages were negative for tubercle bacilli.

November 1952. Improvement maintained. All examinations remain negative for tubercle bacilli and streptomycin was discontinued. X-ray showed slight diminution in the size of the cavity with absorption of the medium (Fig. 20).

December 1952. The patient was discharged from hospital and is required to report as an out-patient for follow-up examinations every month.

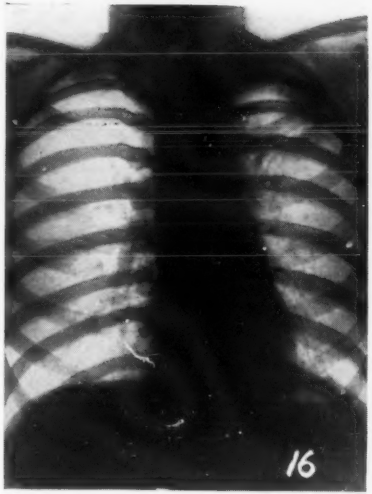
CASE 3. An Indian female, aged 28 years, married, with two children.

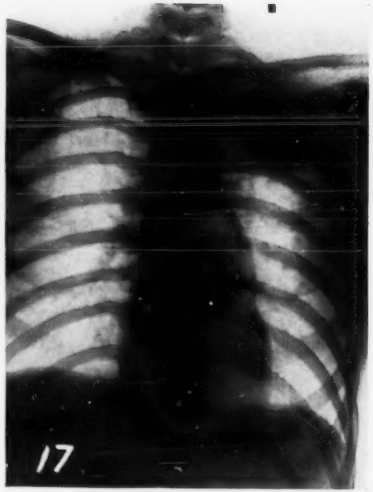
February 1951. She was admitted to hospital with a six months' history of respiratory illness. X-ray showed tuberculous cavitation in the right upper lobe. There was bronchogenic spread of the disease throughout the remainder of the right lung, and to a lesser extent in the middle and lower lobes of the left lung (Fig. 21). She was in a very poor condition, febrile and toxic and had a tuberculous laryngitis. She weighed 85 lb., her E.S.R. was 25 mm./hour and her sputum was heavily infected with tubercle bacilli.

June 1952. After sixteen months of hospital treatment on postural bed-rest, streptomycin and P.A.S. augmented by pneumoperitoneum, she showed considerable improvement. The laryngitis resolved, she gained weight to 100 lb., and her E.S.R. was 20 mm./hour.

X-ray showed considerable clearing of the disease in both lungs, but there was no change in the cavitated right upper lobe (Fig. 22). Her sputum remained positive.

Improvement having been readily gained up to this point, her condition then tended to remain static. Surgical resection of the right upper lobe was considered but, in view of the recent extensive disease elsewhere, it was felt





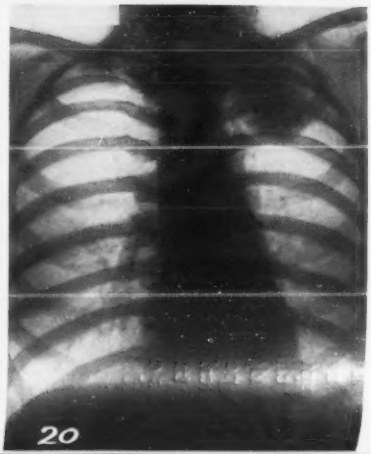


FIG. 16.—*March* 1952.

FIG. 17.—*April* 1, 1952.

X-ray photographs of Case 2, showing tuberculous cavitation in the left upper lobe before and after treatment by injection.

FIG. 18.—*April* 18, 1952.

Left hæmothorax complicating intracavitary injection.

FIG. 19.—*May* 29, 1952.

Showing narrow area of pneumonitis around cavity and clearing of hæmothorax.

FIG. 20.—*November* 1952.

Final X-ray photograph of Case 2 before discharge, showing some diminution in cavity size with absorption of the medium and clearing of the remaining lung fields.

that she was not yet ready for this form of treatment and intracavitary injection was suggested as an interim procedure.

June 17, 1952. Intracavitary injection was performed. Fifteen c.c. of the medium were injected, at which point air could no longer be aspirated from the cavity. The communicating bronchus had been shown to be partly occluded beforehand, and although it was anticipated that at least 30 c.c. would be required to fill the cavity, the procedure was discontinued pending reassessment. Subsequent X-ray showed incomplete filling of the cavity, with a horizontal level of the medium lying loose in the cavity and overlying the position of the communicating bronchus.

Pus aspirated from the cavity before injection of the medium was found to be heavily infected with tubercle bacilli.

July 24, 1952. The right upper lobe cavity was treated by a second injection. On this occasion a further 30 c.c. of the medium were injected until displaced air could no longer be aspirated, whereupon a final small injection was attempted to endeavour to occlude permanently the communicating bronchus. As a result of this latter procedure it was possible to force the medium into the partly occluded bronchus and through to the main bronchus, some of the hardened overflow medium being coughed up.

After withdrawal of the needle the patient was quite comfortable and had no inclination to cough. However, auscultation of the chest elicited coarse rhonchi on the right, and precautionary bronchoscopy was considered advisable. This was carried out and resulted in the removal of a large piece of set medium lying loosely in the right main bronchus and unable to pass between the vocal cords.

Material aspirated from the cavity during the second operation was examined and found to contain tubercle bacilli, but the numbers present in the smear examined were markedly fewer than in the specimen examined from the first procedure.

A subsequent penetrated X-ray taken with a Lysolin grid showed the extent of the cavity to be larger than was expected and the medium to have completely obliterated the cavity space (Fig. 23).

August 1952. One month after completion of treatment the sputum, gastric lavage and bronchial lavage examinations were all negative for tubercle bacilli on direct and cultural examination. Material removed from the wall of the treated cavity by needle biopsy was submitted to similar examinations and found to be completely sterile both for tubercle bacilli and for secondary organisms on direct and cultural examination and on guinea-pig inoculation.

Ordinary P.A. X-ray of the lungs at this stage showed the right upper lobe to be obscured by the contained medium (Fig. 24).

October 1952. The patient's general condition had much improved. She had gained weight to 112 lb., and her E.S.R. was 17 mm./hour. All examinations for tubercle bacilli remained negative.

X-ray showed improvement in both lung fields and decrease in the size of the cavity with absorption of the medium. Since the commencement of intracavitary treatment postural bed-rest, streptomycin 1 gram every third day, P.A.S. and pneumoperitoneum has been continued.

November 1952. Improvement maintained. Posture and bed-rest discontinued and the patient allowed up to commence full-time rehabilitation and occupational therapy.

December 1952. There was very marked improvement in the patient's general condition. She had continued to gain in weight and well-being, and

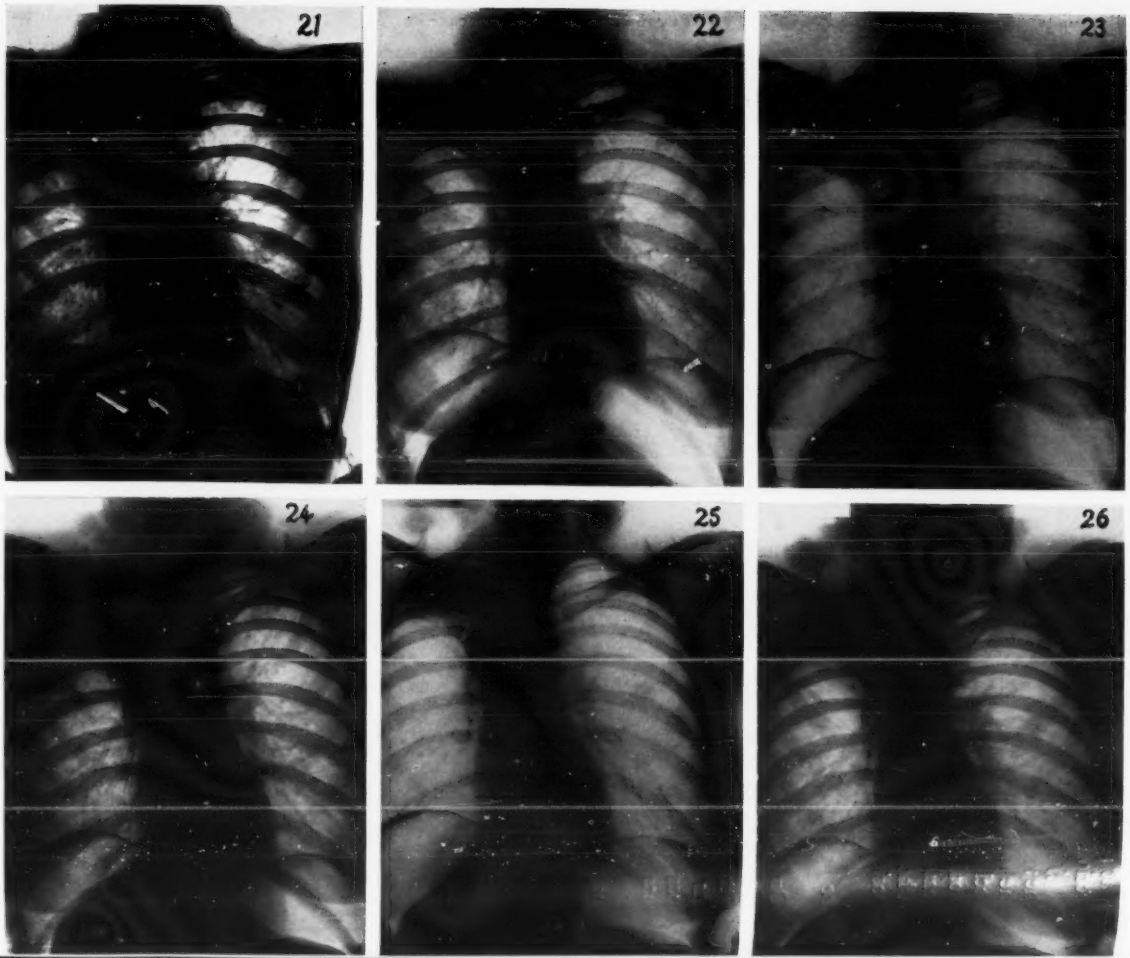


FIG. 21.—*February* 1951.

FIG. 22.—*June* 1952.

X-ray photograph of Case 3, showing, on admission, right upper lobe cavitation with a fluid level and bilateral bronchogenic spread, and the response to treatment after sixteen months.

FIG. 23.—*July* 24, 1952.

Penetrated X-ray taken with a Lysolin grid, showing details of filling of right upper lobe cavity after completion of treatment.

FIG. 24.—*August* 1952.

Ordinary X-ray after treatment, showing right upper lobe obscured by contained opaque medium.

FIG. 25.—*December* 1952.

FIG. 26.—*December* 1952.

Penetrated X-ray (25) and ordinary X-ray (26) for comparison with plates (23) and (24), showing extent of cavity closure, medium absorption and improvement in the remaining lung fields.

her E.S.R. was now 12 mm./hour. Examination of the sputum, gastric lavage and bronchial lavage remained negative for tubercle bacilli. X-ray, penetrated X-ray and tomography indicated marked improvement in both lung fields with closure of the cavity and absorption of the medium by approximately two-thirds of the original size and quantity of medium (Figs. 25, 26 and 27).

The condition of the patient is at present such that she would now be acceptable for surgical resection of the right upper lobe. However, subject to her maintained improvement and well-being, the necessity for this operation is no longer indicated and in any case will be postponed indefinitely in order that in time the end results of intracavitary injection in her case may be observed.

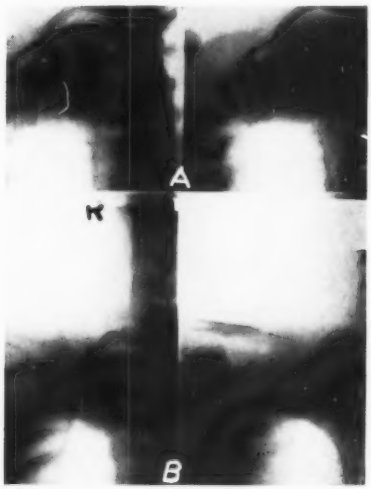


FIG. 27.—Photograph of approximated tomograms of August 1952 (A), and December 1952 (B), demonstrating extent of diminution in size of right upper lobe cavity with absorption of the medium.

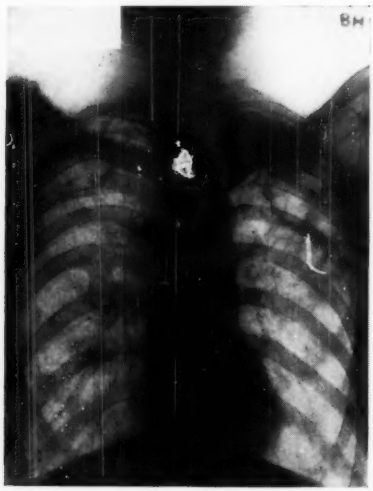
Discussion

The cases described are three on whom the operation of intracavitary injection was performed earlier on in the period under review. They were selected to demonstrate the results obtained, to date, in every case following successful injection of the cavity, and, in Cases 2 and 3, to convey some impression of the course of the procedure and two ensuing complications, viz., hæmothorax and bronchial obstruction requiring immediate post-operative bronchoscopy.

Case 1 describes the first case to receive this form of treatment. At that time no supplies of I.N.H. were available, therefore this preparation was not included in the antibiotic content of the medium. However, the results in this case are as satisfactory as in later cases in which I.N.H. was included.

Close examination of the final X-ray photographs and tomograms of Case 1 will indicate that the left upper lobe cavity has not decreased in size proportionately to the amount of medium absorbed, and that there is a space between the medium and the walls of the cavity. The explanation for this is that the

chronic cough resulting from the residual scarring from the old tuberculous laryngitis had unblocked the communicating bronchus leading to the cavity. Coughing now forced air along the bronchus and into the cavity, causing separation of the walls of the cavity from the medium. The cavity, its original size indicated by the remaining bulk of the medium, now began to enlarge once more. Careful observation of the cavity over a period of one month, during which coughing was rigorously suppressed, has indicated no further increase in in size, but there has been failure to close down on the contained medium. Material aspirated from this cavity, and bronchial lavage, remain sterile for tubercle bacilli. It is therefore apparent that, while the communicating bronchus remains patent, thus allowing atmospheric pressure to exist within the cavity, its further closure will not be obtained, whereas coughing will



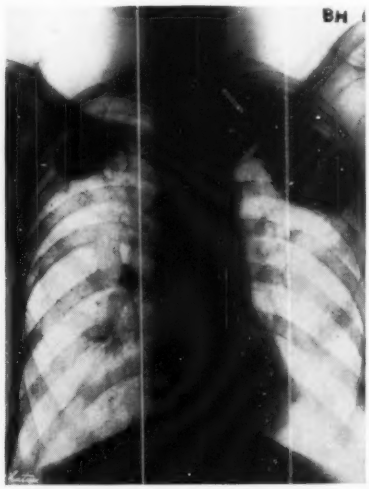


FIG. 28.—Showing left " apicolysis " and downward displacement of the left upper lobe cavity.
FIG. 29.—Showing the same case as Fig. 28, after injection of both upper lobe cavities and left apicolysis.

tend to increase its size. Furthermore, the pooling and stagnation of secretions within the cavity space will encourage the growth of bacteria, although since treatment, and up to the present, tubercle bacilli cannot be demonstrated from that locality. Therefore, before this patient is finally discharged, a further injection will be made into the cavity to obliterate its remaining space and once more occlude the communicating bronchus. In the meantime, measures are being taken to suppress laryngeal irritability and to encourage the patient to give up smoking.

The Indications for Intracavitary Injection.—As this form of treatment develops, and as its potentialities become more apparent, so no doubt will the indications for its application be increased. For example, a limited left " apicolysis " by intrapleural plombage with the ground-nut oil medium was procured in one case. This resulted in depression of the apex of the lung and easier accessibility

of its contained cavity for later injection (Figs. 28 and 29). A modification of the treatment is contemplated in the case of a patient in whom the left upper lobe is honeycombed by multiple small cavities, individual injection into each being impossible. Unsuitable for thoracoplasty, intrapulmonary injection combined with intrapleural plombage is contemplated to compress and obliterate the honeycomb spaces in the lobe.

The sterilising effect brought about in tuberculous lung cavities following treatment by injection has led to a further development. In this respect, by a modification of the medium and technique, work on intrapulmonary injection into non-cavitary localised tuberculous foci is proceeding.

At the present time the indications upon which cases are selected for intracavitary injection are the following:

(1) Long-standing chronic tuberculous cavities, unilateral or more especially bilateral, in the treatment of which major surgery in any form is not suitable, and in which there has been no satisfactory response to a fair trial of other methods of current anti-tuberculous therapy.

An exception to the above is made in cases of single unilateral cavities where surgical resection is ultimately contemplated. The indication here is when such cases are slow to respond adequately to antibiotic therapy owing to the presence of the open secreting cavity, and the risk of bronchogenic spread before resection can be carried out. Case 3 is an example of this exception.

(2) Cases of tension cavitation failing to respond to non-surgical therapy. In this respect the Monaldi method of cavity drainage is replaced, with successful results, by intracavitary injection and bronchial occlusion. The effect of such treatment is illustrated in Case 1, in which the cavity in the left upper lobe indicated by its behaviour, by radiography and by manometer pressure readings that it was a tension cavity.

(3) Cases of severe hæmoptysis, when the source of the bleeding can be traced to a known cavity which is then injected as an emergency measure. This method has, to date, provided an effective form of treatment in two cases, both with extensive bilateral cavitation and hæmorrhaging profusely. In both the bleeding was abruptly terminated and has not recurred. Without treatment the prognosis in such cases is usually hopeless, and death ensues within a short period. Treatment was therefore carried out as an emergency measure and the precaution of ensuring pleural symphysis beforehand ignored.

Contra-indications for Intracavitary Injection.—Contra-indications recognised up to the present are based on the experience of accidents following needling of the chest and lung tissue in this series of cases.

(1) *A Free or Potential Pleural Space.*—In the first few cases treated by intracavitary injection the precaution of first obtaining pleural symphysis was not carried out. The instruments and method of injection were originally so designed that air could not gain entry into the chest from without.

The four procedures required to fill the three cavities in Cases 1 and 2 were carried out without first testing for and ensuring pleural symphysis. In Case 1 no complication occurred, but Case 2 developed a hæmothorax which eventually resolved.

In three cases a partial pneumothorax was induced. In each pleural symphysis had been attempted, but the extent of symphysis obtained was

inadequate. These cases emphasised the need for improvement and greater care in the technique for retesting for free pleuræ after attempted symphysis. In each case either the exploring needle or the injection needle had penetrated the cavity, and the pneumothorax was induced not from the outside but by coughing, which forced air along the needle track from the cavity into the pleural space. Fortunately no case developed a complicating tuberculous empyema.

In another case of an elderly and debilitated European male patient symphysis was inadequate, and, on account of failure in some part of the technique, the medium was injected into the pleural space. The granular antibiotic content of the mixed medium is highly irritating to the pleuræ, which in this case was known to be most sensitive. The irritation of the parietal pleura caused prolonged and acute pain. Bilateral reflex bronchospasm and pulmonary œdema followed and the patient died as a result of ensuing acute cor-pulmonale. This, and another fatality encountered in this series, led to the recognition of another relative contra-indication.

(2) *Extreme Debility or Excessive Loss of Respiratory Function.*—This is a relative contra-indication as indicated by the case just described. During the operation there is a danger of the liquid medium overflowing from the cavity into the main bronchus, setting, and blocking off a bronchus leading to functioning lung tissue elsewhere. Normally the average patient is able to dislodge this obstruction by coughing. A European female was treated by apparently successful intracavitary injection. Seventy-two hours later she suddenly became acutely dyspnœic, cyanosed, and died ten minutes later. She was elderly and debilitated owing to severe disease, and at autopsy her left lung was shown to be almost completely cavitated and functionless. There was disease in the right lung and she suffered from gross intestinal tuberculosis. A large piece of set medium was lying loosely in the trachea opposite the right main bronchus, which was considered to have been suddenly obstructed. Normally such an obstruction could have been dislodged, but the patient was too debilitated to do so and died of acute respiratory insufficiency.

Although the prognosis in the above case was hopeless, intracavitary injection was performed with a view to alleviating the intestinal condition by reducing the amount of infected pulmonary secretions passing into the intestinal tract.

Such cases as the two described above will require special assessment and consideration before intracavitary injection is finally decided upon, and the procedure and after-care are carried out with such factors constantly in mind.

(3) *A Prothrombin Index of less than 70 per cent.*—The wide-bore injection needle has on one occasion entered a large blood vessel and been withdrawn. No obvious complications ensued, although pulmonary hæmatoma or hæmosiderosis were anticipated. The sharp cutting point of the original 13-gauge needle before adaptation is purposely squared off, bevelled, and fitted with a blunt stilette. Thus lung tissue, blood vessels and other structures in the chest liable to penetration are punctured rather than pierced, and bleeding is reduced to a minimum.

(4) *Inadequate Facilities.*—This is mentioned in view of the fact that without adequate facilities in respect of X-ray, fluoroscopy equipment and theatre facilities for bronchoscopy at short notice, the procedure becomes increasingly

difficult and may endanger the life of the patient. It is felt that the operation should be undertaken only in institutions specialising in diseases of the chest, where facilities and equipment for major chest surgery are available.

Factors influencing the Outcome of Intracavitary Treatment.—Up to the present, and subject to the above indications, the nature of the tuberculous cavity in respect of size, shape or situation, or the ultimate prognosis of the patient, have not influenced the selection of cases for intracavitary treatment. Multiple honeycomb cavities are an exception. These are technically difficult if not impossible to fill completely. The smallest cavity treated to date required 15 c.c. of the medium to fill it, the largest required over 300 c.c.

Undoubtedly the most satisfactory results are obtained in the treatment of the smaller cavities, more especially when these are situated in the upper lobes or their apices. Furthermore, it has been found that prolonged maintenance of pneumoperitoneum with postural bed-rest after treatment improves these results. The congestion of the upper lobes so caused favours closure of the cavity and absorption of the medium, against which better contact and compression by the surrounding lung and cavity walls are maintained.

The most suitable cases have so far been found to be those where a cavity is situated in a contracted right upper lobe, of which Case 3 reported earlier is a typical example. The reason for this is not yet fully understood, for this so-called " upper lobe syndrome " is thought to be due to a greater tendency to kinking and obstruction of the upper lobe bronchus and a less efficient blood supply to the upper lobe as compared with the rest of the lung. In Case 3 and in several other cases with right upper lobe cavities in whom intracavitary treatment was undertaken in this series, a partially stenosed communicating bronchus was identified on preliminary investigation of the cavity. However, where the blood supply to a lobe of the lung is less efficient, one would expect delayed absorption of the medium, yet in right upper lobe cavities treated to date the opposite has been demonstrated.

Although the advantages of sputum conversion and sterilisation of the cavity are obtained, many of the larger cavities treated have, up to the present, demonstrated little or no obvious absorption of the medium with closure of the cavity. This is attributed to the greater mobility of the larger bulk of the medium within the cavity, thus delaying or preventing the firm adherence of the medium to the cavity wall. Without exception, large cavities that have demonstrated closure and medium absorption have all been present in upper lobes of patients whose behaviour and co-operation after treatment has been the most satisfactory. In this respect the strict maintenance of postural bed-rest for at least two months, with the minimum of walking about or movement in bed, has produced the most beneficial results.

With the exception of those cavities treated for hæmoptysis, 31 cavities have received successful treatment by injection. Where more than 80 c.c. of the medium are required, such a cavity is regarded as large, a small cavity requiring less than this amount. Of the 31 cavities treated, 27 were in the upper lobes, 15 in the left and 12 in the right. In the left upper lobe 6 were large cavities, of which 2 have to date shown evidence of closure, and 9 were small, 4 showing closure. In the right upper lobe 5 were large and 7 small, of which 1 and 5 respectively have shown evidence of closure. Three large cavities have been

treated in the left lower lobe, one of which was in the dorsal segment, and one in the dorsal segment of the right lower lobe. Of the lower lobe cavities only one in the left has been found to have decreased in size. The 13 cavities showing evidence of closure to date are not a full reflection of this result of treatment. In most cases at least two months or more must elapse between treatment and the first indication of closure and medium absorption, and it is expected that, in due course, the remaining cavities, especially the smaller ones, will indicate response in respect of closure. The cavities indicated above as showing evidence of closure have all been of five months' standing or more after treatment.

An unexpected feature encountered following the induction of a chemical pleuritis for pleural symphysis is deserving of comment:

One or two months after the intrapleural injection, and before intracavitary injection was carried out, several patients showed a decrease in size of long-standing chronic cavities which up to that time had failed to respond to any other form of treatment. This feature may have been coincidental, but it occurred in a sufficient number of cases to evoke comment and require an explanation.

Two theories are offered in explanation of this reaction to a chemical pleuritis, the first of which is considered the most likely:

The great majority of patients selected for intracavitary treatment have been hospital patients for a period of at least two years. After this time they are restless and in a low state of morale. They have observed or heard of the improvement and subsequent discharge of other long-standing patients following intracavitary injection, and when the recognised preliminaries of this new form of active treatment are applied to themselves, they at once become more optimistic and co-operative in maintaining more efficient postural bed-rest, with corresponding improvement in their pulmonary disease.

The second theory offered is based on the observation that most of the patients exhibiting this feature of cavity closure did so following the induction of a chemical pleuritis accompanied by some degree of pleuritic pain requiring sedation. All these patients were receiving antibiotic therapy in one form or another at the time. It is therefore suggested that the pleural irritation induced leads to a pleural hyperæmia, which, in respect of the visceral pleura, is derived from increased vaso-dilatation and correspondingly increased blood flow from the diseased lung of that side in response to the pleural irritation. Thus bloodborne antibiotics are more readily available to that lung and its contained disease.

From the second explanation one is led to suggest a clinical trial of a variation in the treatment of pulmonary tuberculosis. This would be the concurrent oral and parenteral administration of anti-tuberculous drugs together with the intrapleural injection of those same drugs in solution with a chemical irritant. In this manner, if the second theory is substantiated, a higher concentration of drugs would become available to the diseased lung via its increased circulation in response to the pleural irritation, and later via the proportionate reabsorption by the visceral pleura of the ensuing pleural exudate and its antibiotic content.

The Complications following Intracavitary Injection.—Only complications actually experienced to date in this series of cases will be mentioned, although

the possibility of others is recognised. The majority have already been mentioned in the foregoing discussion.

(1) *Blood-staining of the Sputum.*—This occurs not infrequently after needling lung tissue. It has always been slight, transient and of no consequence. However, the patient should be warned of its possible occurrence and reassured.

(2) *Pyrexia.*—A slight pyrexia in reaction to the procedure is common. Pyrexia persisting over twenty-four hours or higher than 101° F. is taken to indicate an underlying complication if the patient was previously afebrile.

(3) *Expectoration of Bronchial Casts.*—Excessive coughing or bronchial irritation is not common after intracavitary injection. However, several patients in whom the bronchus draining the cavity has been long and thoroughly occluded by the medium have, for some time afterwards, expectorated small bronchial casts broken off from the main mould in the bronchus. Case 1 reported above succeeded in completely unblocking the communicating bronchus, allowing air to re-enter the cavity.

(4) *Bronchial Obstruction.*—This complication has received adequate description in the foregoing discussion, case reports and account of the technique. It has occurred on three occasions in this series, causing the death of one patient, and remedied by bronchoscopy in the other two. Unless indicated, bronchoscopy is not carried out as a routine after intracavitary injection. Once the medium is set in the cavity the patient is encouraged not to cough and to lie still for at least an hour. Thus the medium, although no longer in the liquid state, in undergoing complete setting is assisted in moulding itself to the shape of the cavity. Thus coughing inevitably induced by endobronchial instrumentation is not considered favourable towards the ultimate success of the treatment.

(5) *Failure to locate the Cavity.*—Those cavities which so far could not be located on exploratory needling of the lung have all been larger than 1½ inches in diameter, radiologically obvious, and apparently easy to locate, whereas small cavities of 1 inch in diameter or less have been successfully located. The impression gained is that this may be accounted for by the fact that these cavities are partly or completely inspissated with caseous material, itself not obvious on X-ray, and through which the point of the needle passes without free aspiration of air to indicate its presence in the cavity. Such cavities are demonstrated at autopsy, where X-ray demonstrates the fibrous lining of the wall of the cavity. The latter, when opened, is found to be filled with caseous material.

Other cavities have peculiarities in shape, although appearing spherical on X-ray. These may be flat, " dumb-bell," or saucer-like in shape, through which the needle may pass without free aspiration of air.

(6) *The Presence of Liquid Pus in the Cavity.*—When a cavity is found to contain a considerable quantity of liquid pus the medium cannot be injected. Instead of setting in a solid mass, the medium solidifies in separate small lumps surrounded by liquid pus and, eventually, itself becomes liquefied. As a preliminary to injection such cavities must be drained empty by postural drainage or needle aspiration of the pus if such is possible.

(7) *Needling of a Large Blood Vessel.*—Such an occurrence is disturbing to the operator, especially when blood is seen passing along the tube leading to the

manometer, the steadily rising positive pressure of which is at first somewhat puzzling. For this reason it is recommended that the sterile extension rubber tubing to the manometer be translucent.

As a matter of principle, no open-ended needle is permitted to remain in the chest at any time during the operation. Needling of the chest is always carried out under a closed system by attachment of a syringe, stilette or manometer. In this way the accidental puncture of a large low-pressure blood vessel in the chest is not followed by intravascular aspiration of air during inspiration.

(8) *Pneumothorax.*

(9) *Hæmothorax.*

(10) *Medium unintentionally entering the Pleural Space.*—(8), (9) and (10) above have already been discussed under pleural symphysis and contra-indications. They are due to failure in obtaining adequate pleural symphysis, and (10) has led to the second of the two deaths encountered in this series and already described.

(11) *Surgical Emphysema.*—This occurred in one case when coughing forced air along the needle track into the subcutaneous tissues of the anterior chest wall. The future prevention of this complication is attempted by the injection of the medium for a short distance along the needle track as the needle is withdrawn from the chest.

The above complications are concerned mainly with the actual operation and technique of intracavitary injection. To date there have occurred only two complications following successful technical filling of the cavity. These, though troublesome, are not of a serious nature and may be avoided.

(12) *Accumulation of Pus in a Treated Cavity followed by the Medium becoming liquefied.*—The case in which this occurred is fully described.

CASE 4. An Indian female, aged 25 years, unmarried.

June 1951. Admitted to hospital with extensive tuberculous infiltration of the whole of the left lung and cavitation in the left upper lobe. There was early spread of the disease to the right lung and gross endobronchial tuberculosis with ulceration. Her sputum was strongly positive.

She was treated by postural bed-rest, streptomycin and P.A.S., and in February 1952 an anterior thoracoplasty with removal of the anterior ends of the second and fifth ribs was performed. This operation was intended as a preliminary to anterior Monaldi drainage of the cavity to be later followed by a total left thoracoplasty. Owing to inadequate clearing of the disease on the right and to constant spread from the left upper lobe cavity this programme was delayed. In the meantime intracavitary injection was contemplated to arrest further spread of the disease from the cavity.

June 27, 1952. The patient was treated by intracavitary injection into the left upper lobe. The cavity was completely filled, and at the conclusion of the operation only a small quantity of hardened medium was coughed up, indicating occlusion of the bronchus. Figs. 30 and 31 indicate the X-ray and tomogram appearance of the cavity and lungs before treatment, and penetrated X-ray after treatment (Fig. 32) gave no reason to suggest that the cavity was other than successfully filled. There was no reaction or pyrexia after treatment, the patient was quite comfortable, and there was no indication for bronchoscopy.

July 27, 1952. There was some improvement in the patient's general con-

dition, and sputum examination at this time was negative for A.F.B. for the first time since her admission to hospital. The patient was comfortable and complained of nothing unusual to indicate unexpected pathology in the chest. Her temperature for the last month had been essentially normal. However, the most recent routine X-ray examination of the chest (Fig. 33), indicating the opaque medium to be resting in a cavity twice its original size, was unexpected. It was thought at this time that the communicating bronchus had opened by dislodgement of the occluding medium, and that the medium remaining in the cavity had acted as a ball-valve at the point of entry of the bronchus into the cavity, and that the latter had subsequently " blown up " with air.

Insertion of a needle into the cavity failed to locate any air whatsoever, but instead approximately 60 c.c. of yellow-green liquid pus was aspirated. Culture of this pus failed to grow tubercle bacilli, and guinea-pig inoculation of the material produced no result after six weeks, when the animal was killed. Subsequent X-ray after aspiration showed the cavity to be once more closed down about the contained medium.

August 3, 1952. The patient complained of a wheezing noise in her left chest whenever she took a deep breath. X-ray showed the cavity to have again increased in size. On this occasion needling of the cavity indicated the presence of air, and that the communicating bronchus was now patent, for aspiration of air from the cavity produced an audible wheezing as air re-entered via the stenosed bronchus, now incompletely occluded. A further 15 c.c. of sterile pus was on this occasion aspirated from the cavity.

August 14, 1952. X-ray indicated a fluid level in the enlarged cavity (Fig. 34). Further needling disproved it to be a tension cavity as the intracavitary pressures ranged between minus 4 and plus 4, and the communicating bronchus was now shown to be widely patent. Material was aspirated from the cavity and found to consist of a mixture of sterile liquefied medium and pus. The patient's sputum had in the meantime remained negative for tubercle bacilli.

The explanation of the events described in Case 4 is as follows: From the appearance of the cavity before treatment it would appear to be approximately $1\frac{1}{2}$ inches diameter in size, whereas in actual fact its true size is indicated in plate 34 to be approximately $3\frac{1}{2}$ inches in diameter and occupying almost the whole of the left upper lobe. The cavity before treatment was almost completely filled with caseous material lining its walls, leaving a small space leading via a channel through the caseous material to the communicating bronchus. The presence of the medium in this space acted as a foreign body and rapidly converted the caseous material into liquid pus, and by some interaction with the pus, probably enzymic, the medium became dehydrogenated and reverted to the liquid state.

It is necessary to recognise the character of such cavities by radiological examination and exploratory needling of the cavity walls for the presence of excess caseous material. To date two other such cavities have been identified by these methods, and, prior to the instillation of the medium, these have been subjected to the following preliminary treatment:

By the same technique as for Monaldi cavity intubation, but using a smaller trochar and cannula, a length of size No. 2 Polythene tubing is inserted through the chest wall into the cavity. The tube is prevented from becoming blocked by secretions by the permanent insertion of an equal length of thin, doubled

FIG. 30.—*June* 27, 1952.

FIG. 31.—*June* 27, 1952.

Case 4: X-ray photographs showing left upper lobe cavity, left anterior thoracoplasty and spread of disease on the right (Fig. 30) and tomograms of the cavity at 7 and 9 cm. (Fig. 31).

FIG. 32.—*June* 27, 1952.

FIG. 33.—*July* 27, 1952.

X-ray photographs showing complete filling in 32 c, and the greatly enlarged cavity and contained medium one month later (Fig. 33).

FIG. 34.—*August* 14, 1952.

Showing true size of left upper lobe cavity after complete liquefaction of the lining caseous material together with the medium, forming a fluid level within the cavity.

and flexible silver fuse wire. After a period of seven days has elapsed, during which the sinus should have healed and granulated to prevent subcutaneous emphysema from the cavity, further treatment is commenced. Daily intracavitary injections are made through the tube of solutions of streptomycin, P.A.S. and I.N.H., alternating with lytic agents such as Streptokinase-Dornase, Tryptar and others. In this manner the caseous material is liquefied and evacuated from the cavity by controlled postural drainage via the communicating bronchus. Following this preliminary " physiological curettage " of the cavity, eventual treatment by injection of the medium is possible after healing of the sinus track.

Two cavities have, up to the present, been treated in this manner. Apart from an increased purulent sputum output, no undesirable effects have been forthcoming following the use of the draining bronchus for evacuation of the liquefied contents.

(13) *Evacuation of the Solid Medium from the Treated Cavity.*—The single incidence of this complication should normally not have occurred.

Almost the total area of the left lung of an Indian male patient was occupied by two large tuberculous cavities which were completely filled by injection of over 450 c.c. of the medium, requiring four procedures over a period of two weeks (Fig. 35 and Fig. 9). At this time the I.N.H. was available only in the form of 25 mg. tablets. The sixteen crushed tablets required to constitute the 400 mg. I.N.H. content of the medium rendered the total antibiotic powder content of the medium too great. Thus, when solid, the medium was excessively brittle and unstable within the cavity. Although clinical improvement and sputum conversion were obtained, over a period of two months the patient gradually evacuated the medium from the cavities until they were almost empty (Fig. 36). His sputum conversion was however, maintained, and another interesting feature of this case is that it was possible to introduce a bronchoscope into the lower of the two cavities, and an X-ray was taken of the instrument in this position.

At a later date, requiring four more procedures, the cavities were refilled with the medium, but on this occasion using the same quantity of I.N.H. contained in less bulk. It was observed that on this occasion less total quantity of the medium was required for complete filling than on the first occasion, although radiological evidence of cavity closure was lacking.

The four procedures required for the second filling of the cavities were carried out on four consecutive days, which was a mistake, for the daily cocaine throat spray and bronchial inhalation for four days led to the last and most recent complication encountered in this series.

(14) *Cocaine Poisoning.*—This occurred once in the case of the patient just described, and was due to excessive administration of cocaine inhalation over too short a period. Treatment along the usual lines resulted in complete recovery, and the patient is now well with regard to the cocaine poisoning, and also remains free of evidence of active tuberculosis.

The Incidence of Complications of Intracavitary Injection.—As the principles and procedure for intracavitary injection were evolved, so certain complications were anticipated and modifications made to avoid their occurrence. Once work was commenced on the injection of cavities, as other complications

occurred, so the technique was altered or modified, as were the pre- and post-operative procedures. The result, as indicated in Table No. 2, was that the majority of complications occurred earlier in this series of cases, whereas the procedure and technique in its present form has reduced the incidence of complications to within reasonable and satisfactory limits.

TABLE No. 2

Table to indicate the Decreasing Incidence of Complications as the Technique for Intracavitary Injection was modified between February and November 1952

MONTH	OPERATIONS	COMPLICATIONS
February	1	Nil
March	7	3
April	8	2
May	7	3
June	9	2
July	10	2
August	7	1
September	8	Nil
October	6	Nil
November	3	1
	66	14

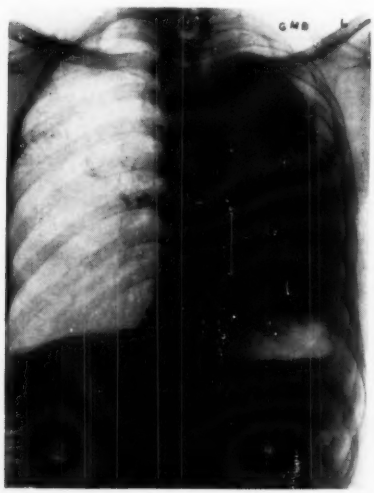


FIG. 35.—*April* 1952.

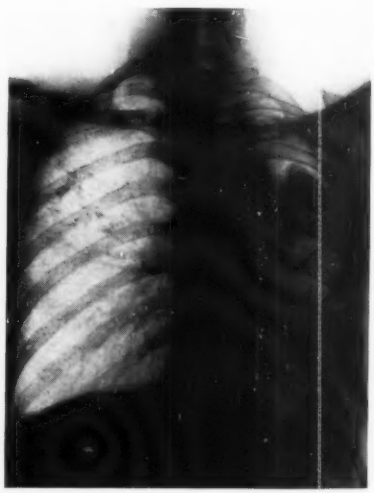


FIG. 36.—*August* 1952.

X-ray photograph of a penetrated plate, showing completed filling of two large tuberculous cavities occupying almost the whole of the left lung (Fig. 35). Four months later (Fig. 36) the medium is shown to be almost completely evacuated with pooling of secretions in the lower cavity. In November 1952 both cavities were successfully refilled.

At each operation a needle is inserted into the chest and lung tissue on at least two occasions. Treatment attempted on a total of 46 tuberculous cavities required 66 operations involving the insertion of a needle into lung tissue approximately 150 times with a total of 14 complications, incurring 2 deaths.

Of these 14 complications, 4 only resulted in failure to inject the cavity. These were due to 2 accidental inductions of an artificial pneumothorax and 2 accidental injections of the medium into the pleural space, one of the latter cases resulting in death of the patient.

The remaining 10 complications were associated with successful technical injection of the cavity, 8 of which did not affect the ultimate success of the treatment as so far obtained in uncomplicated cases. These complications were:

1 accidental induction of an artificial pneumothorax,
3 cases of bronchial obstruction by the medium, 2 of which were successfully remedied by bronchoscopy, the other was not recognised and caused the death of the patient under circumstances already described,
1 hæmothorax which eventually resolved,
1 case of the needle entering a large blood vessel,
1 subcutaneous emphysema which resolved,
1 incidence of cocaine poisoning responding to treatment,
1 case of evacuation of the medium from the cavity, and
1 case of liquefaction of the medium within the cavity owing to the presence of caseous material.

A GENERAL SURVEY OF WORK AND RESULTS OF INTRACAVITARY INJECTION

(*Tables* 3 *and* 4)

Since the commencement of this experimental work on the injection of tuberculous cavities, and during the period under review from February 29 to November 30, 1952, treatment has been attempted on a total of 46 cavities in 38 patients, requiring 66 separate operations.

The patients consisted of 11 European males, 3 European females, 3 Indian males, 5 Indian females, one Coloured male, 13 African males and 2 African females. All were patients of the King George V and Wentworth Hospitals, Durban.

The distribution of tuberculous cavities among these patients was as follows:

	Patients
Single cavities	23
Two cavities	9
Three cavities	3
Multiple cavities	3

In 38 patients, with 46 cavities on which treatment was attempted, 8 cavities in 7 patients were found to be unsuitable for injection. (Of these 2 are undergoing preliminary treatment by cavity intubation.)

Of the remaining 38 cavities in 31 patients, intracavitary injection was carried out in 33 cavities and failed in 5 owing to complications mentioned above.

Nine cavities successfully injected are present in 6 patients in whom other cavities yet remain to be treated and are thus recorded as incomplete cases.

As a result of extensive disease and toxæmia, and unrelated to the intracavitary injections received, death has occurred in one of these cases before treatment could be completed.

Intracavitary injection was carried out as emergency treatment for severe hæmoptysis from 2 cavities in 2 patients. In so far as hæmoptysis was the indication for treatment in these cases, the treatment was successfully applied, but owing to the presence of multiple honeycomb cavities in both cases, further treatment by injection is not contemplated, and sputum conversion and other favourable results cannot be expected.

In the remaining 18 patients, involving 22 tuberculous cavities, treatment has been successfully completed.

TABLE No. 3. *Survey of Treatment by Intracavitary Injection during period February 29–November 30*

	Treatment attempted		
	Cavities treated	*Number of Operations*	*Number of Patients*
Completed cases	22	41	18
Incomplete cases	9	10	6
Found unsuitable for treatment	6	6	5
Preliminary cavity intubation	2	2	2
Failed owing to complications	5	5	5
Treated for hæmoptysis only	2	2	2
	46	66	38

Patients on whom treatment has been completed are submitted to the following routine follow-up examinations:

Monthly examination of the sputum for tubercle bacilli by direct and cultural methods and similar examination of the fasting gastric contents. Monthly X-ray of the chest with tomography of the cavity and monthly clinical assessment including weight and E.S.R. Three-monthly bronchoscopy with cytological examination and direct and cultural examination for tubercle bacilli of material obtained by bronchial lavage.

Of the eighteen patients on whom treatment has been successfully completed, all have converted to and maintained sputum negative for tubercle bacilli on direct and cultural examination, and in all the sputum output has decreased in quantity. All have shown clinical improvement, gain in weight and decrease in the E.S.R. During the period under review thirteen cavities have shown radiological evidence of closure with absorption of the medium, but, as yet, in no case has this been complete. The greatest extent of cavity closure observed to date has been more than two-thirds of the original cavity size in cases of over five months' standing. Where any degree of endobronchial tuberculous disease has been observed before treatment, this has shown improvement to complete resolution after treatment, and direct and cultural examination of the bronchial washings have failed to reveal tubercle bacilli in any of these patients, all of whom were sputum positive before treatment.

TABLE No. 4. *Follow-up Results of 18 Patients successfully treated by Intracavitary Injection*

Maintained sputum conversion (direct and on culture)	18
Bronchial lavage negative for tubercle bacilli	18
Diminution in sputum output	18
Clinical improvement, gain in weight and decreasing E.S.R.	18
Evidence of cavity closure and medium absorption to date	11

Conclusions

In institutions specialising in the active treatment of diseases of the chest, the procedure and technique of intracavitary injection as described may be undertaken with safety in the treatment of chronic tuberculosis of the lungs with cavitation.

The theoretical principles upon which this form of treatment was evolved have been shown to be obtained in practice in those patients successfully treated up to the present time in respect of sputum conversion, failure of any examination to demonstrate the presence of tubercle bacilli, clinical and radiological improvement after treatment, and closure of tuberculous cavities.

A possible exception to the above is cavity closure. It has been shown that smaller cavities in upper lobes exhibit a definite and marked decrease in size with absorption of the medium over a period of five months. However, larger cavities, although the other advantages of the treatment are obtained, do not all exhibit the same tendency to closure as the smaller ones, which is considered to be due to the greater mobility of the larger bulk of contained medium.

Nevertheless, irrespective of cavity closure, a number of patients successfully treated have been discharged from hospital, others are undergoing occupational and rehabilitation therapy, and in none can active tuberculosis be demonstrated. Were it not for this form of treatment these patients would today, as they have for the past two or more years, remain confined to their wards as infectious cases indefinitely occupying a hospital bed.

By following the technique and procedure described, the incidence of major and minor complications may be reduced to an extent where, with the possible exception of needling a blood vessel or bronchial obstruction rectifiable by bronchoscopy, their incidence need be no greater than in other minor procedures in chest surgery.

For these reasons it is felt that this form of intracavitary treatment, although essentially of an experimental nature up to the present, should continue, and be more widely applied towards the treatment and release of those hospital patients with long-standing chronic pulmonary tuberculosis with cavitation.

Summary

A new method of treatment for chronic pulmonary tuberculosis by intracavitary injection is presented.

Theories of tuberculous cavitation and the principles upon which this form of treatment has developed are discussed.

The procedure and technique of the operation are described in detail, together with its present indications and contra-indications, and the complications so far encountered.

A complete survey is given of the results of the application of this treatment to forty-six tuberculous cavities in thirty-eight hospital patients.

REFERENCES

CORYLLOS, P. N. (1936): *Amer. Rev. Tuberc.*, **33,** 639.
STEENKEN, W., D'ESOPO, N. D., and WOLINSKY, E. (1947): *Amer. Rev. Tuberc.*, **56,** 403.
HUNTER, R. A., and PEILL, E. J. (1938): *Brit. J. Tuberc.*, **32,** 136.
DORMER, B. A.: Unpublished personal communication.
HILDITCH, T. P. (1949): " Fats and Waxes."
RICHARDS BOLTON, E., and REVIS, C.: " Oils, Fats and Fatty Foods," 3rd edition.
DUBOS, R. J. (1950): *J. Mount Sinai Hospital*, **17,** 229.
BEEMER, A. G., and DORMER, B. A. (1952): *South African Med. J.*, **26,** 311.
HOBBY, G. L., LENERT, T. F., DONIKAIN, M., and PIKULA, D. (1951): *Amer. Rev. Tuberc.*, **53,** 434
BROCK, R. C. (1948): *Thorax*, **111,** 88.

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